#### PATENT COOPERATION TREATY

TRANSLATION INTERNATIONAL SEARCHING AUTHORITY To: WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1) Date of mailing (day/month/year) FOR FURTHER ACTION Applicant's or agent's file reference See paragraph 2 below ASAHI-49 Priority date (day/month/year) International filing date (day/month/year) International application No. 29.01.2004 27.01.2005 PCT/JP2005/001102 International Patent Classification (IPC) or both national classification and IPC Applicant ASAHI KASEI PHARMA CORPORATION This opinion contains indications relating to the following items: Box No. I Basis of the opinion Box No. II Priority Non-establishment of opinion with regard to novelty, inventive step and industrial applicability Box No. III Box No. IV Lack of unity of invention Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial Box No. V applicability; citations and explanations supporting such statement Box No. VI Certain documents cited Box No. VII Certain defects in the international application Box No. VIII Certain observations on the international application FURTHER ACTION If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered. If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCI/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. For further options, see Form PCT/ISA/220. For further details, see notes to Form PCT/ISA/220. Authorized officer Name and mailing address of the ISA/JP

Facsimile No.

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/001102

| Вох | No. I | Basis of this opinion   |   |                  |                 | <u>,                                     </u> |  |              |                |
|-----|-------|---|---|------------------|-----------------|---|--|--------------|----------------|
| 1.  |       | n regard to the language, this of unless otherwise indicated un                               |   | ed on the basis  | of the internat | ional applic                                  | ation in the la                          | nguage in v  | which it was   |
|     |       | This opinion has been establi   | shed on the basis of a tran                         |                  |                 |   |  |              | arch (under    |
|     | •     | Rule 12.3 and 23.1(b)).   |   |                  |                 | •   |  |              |                |
| 2.  | With  | n regard to any nucleotide anntion, this opinion has been est                                 | nd/or amino acid seque<br>ablished on the basis of: | nce disclosed i  | n the internat  | ional applic                                  | ation and nec                            | cessary to   | the claimed    |
|     | a.    | type of material  |   |                  | ,               |   |  |              |                |
| •   |       | a sequence listing  | •   |                  |                 |   |  |              |                |
|     |       | table(s) related to the s   | equence listing                                     |                  |                 |   |  |              |                |
|     | b.    | format of material  |   | •                |                 |   |  |              |                |
|     |       | in written format   |   |                  |                 |   |  |              |                |
|     |       | in computer readable for  | orm   |                  |                 |   |  | ·            |                |
|     | c.    | time of filing/furnishing   |   |                  |                 |   |  |              |                |
|     |       |   | ational application as filed                        | L.               |                 |   |  |              | ·              |
|     |       | <del>-</del>  | international application is                        |                  | lable form.     |   |  |              |                |
|     |       | <b>—</b>  | to this Authority for the p                         |                  |                 |   |  |              |                |
|     | _     |   |   |                  |                 |   | ور د در | b            | haan filad ar  |
| 3.  | L     | In addition, in the case that<br>furnished, the required state<br>filed or does not go beyond | ments that the information                          | n in the subsequ | ent or addition | and/or table<br>nal copies is                 | identical to the                         | hat in the a | application as |
| 4.  | ۸dd   | litional comments:  |   |                  |                 |   |  |              |                |
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|     |       |   |   |                  |                 |   |  |              |                |

### WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/JP2005/001102

|   | =:   |  | CHING AUTHORITY   | PCT/JP2005/001102   |               |
|---|--|--|---|---|---------------|
| Box No. V Reasoned statement under Ru<br>citations and explanations sup |  |  | ulc 43bis.1(a)(i) with regard to novelty, invent  | ive step or industrial applicability;   |               |
| 1.  | Statement  |  |   |   | _             |
|   | Novelty (N)  | Claims   | 1-4   | YES   | s             |
|   |  | Claims   |   | NO  | 1             |
|   | Inventive step (IS)  | Claims   |   | YES   | s             |
|   |  | Claims   | 1-4   | NO NO   | ,             |
|   | Industrial applicability (IA)  | Claims   | 1-4   | YE:   | s             |
|   |  | Claims   |   | NO NO   | )             |
| 2.  | Citations and explanations:  |  |   |   |               |
|   | Claims, Industrial Field  Document 2: JP, 61-152 Claims, Industrial Field  Document 3: US, 2003/2 Claims 1-4 Claims 1-4 do n  ISR. Document 1 or sulfonic group as an age like. Document 3 des cardiovascular diseases describe that inflammat diseases, and that vasod The subject mat and treatments for cardi same drug may be appli fasudil can be used for t used in conjunction with | of Invention of Invention of Invention 162824, of appear 2 describer a related to infection accoulators of dovasculated to infection other describer of dos describer of the prevention other describer of describer of the prevention other describer of describer of describer of the prevention of the pr | (Asahi Chemical Industry Co., Ltd., ation, page 2, lower left column, co.) (Asahi Chemical Industry Co., Ltd., ation, page 5, upper left column, co.) A1 (Elaine S. Krul et al), 28 April, ar to involve an inventive step in vious the effectiveness of an isoquino are prevention of and treatments for an agent and composition for the presonant properties in the same documents 1-3 involve a common to are diseases. Therefore, from the destination of and treatments for cardiovalrugs.  (Asahi Chemical Industry Co., Ltd., ation, page 2, lower left column, co.)  A1 (Elaine S. Krul et al), 28 April, are to involve an isoquino an agent and composition for the preson and the presentation of and treatments for cardiovalrugs.  (Asahi Chemical Industry Co., Ltd., ation, page 2, lower left column, co.)  A1 (Elaine S. Krul et al), 28 April, are to involve an isoquino and treatments for the presentation of and treatments for cardiovalrugs. | mpound (1)  ), 11 July, 1986 (11.07.86), mpound (60)  2003 (28.04.03), Claims  ew of documents 1-3 cited in the line derivative containing a vascular dilation, angina and the evention of and treatments for ygenase 1.Therefore, claims 1-4 luded among cardiovascular id method. echnical field for the prevention of cription of document 3, while the soperation, it can be seen that rascular diseases, albeit it has to be it in the art could have easily | of<br>e<br>be |
|   | sulfonic group described cardiovascular diseases.  | d in docu  | ument 1 or 2 for the prevention of a  | no treatments for inflammatory  |               |
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### PATENT COOPERATION TREATY

| From the<br>INTERNATIONAL SEARCHING AUTHOR!  | ITY ·  |  | TNS,   |
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| То:  |  |  | PCT  |
|  |  |  | RITTEN OPINION OF THE IONAL SEARCHING AUTHORITY  (PCT Rule 43bis.1)  |
|  |  | Date of mailing (day/month/year)   |  |
| Applicant's or agent's file reference ASAHI-49   |  | FOR FURTHER  | See paragraph 2 below  |
| International application No. PCT/JP2005/001102  | International filing date 27.01.2005   | (day/month/year)   | Priority date (day/month/year) 29.01.2004  |
| Applicant ASAHI KASEI PHARMA CO  | RPORATION  |  | ,  |
| Box No. IV Lack of unit  Box No. V Reasoned st applicability  Box No. VI Certain doc  Box No. VII Certain defe  Box No. VIII Certain obse  2. FURTHER ACTION  If a demand for international prelinternational Preliminary Examining than this one to be the IPEA and the this International Searching Authority  If this eminion is as provided above. | shment of opinion with restry of invention satement under Rule 43bis critical critical and explanation uments cited exist in the international approximation on the international explanation of the internation of the international explanation in the internation in the international explanation in the international explanation in the internation in the in | egard to novelty, inventors. I(a)(i) with regard to one supporting such states application on all application on that this does not apply that this does not apply the international Burd.  Justice of the legislation of the IPE, before the expiration | ill be considered to be a written opinion of the ply where the applicant chooses an Authority other reau under Rule 66.1 <i>bis</i> (b) that written opinions of A, the applicant is invited to submit to the IPEA and a months from the date of mailing of Form |
| Name and mailing address of the ISA/JP   | <u></u>  | Authorized officer   |  |
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Facsimile No.

# WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2005/001102

| Вох | No. I          | Busis of this opinion  |                       |
|-----|----------------|--|-----------------------|
| 1.  | With<br>filed, | regard to the language, this opinion has been established on the basis of the international application in the languages otherwise indicated under this item.  | page in which it was  |
|     |                | This opinion has been established on the basis of a translation from the original language into the following language.  |                       |
|     |                | , which is the language of a translation furnished for the purposes of internal  | nonai scarch (under   |
|     |                | Rule 12.3 and 23.1(b)).  | eary to the claimed   |
| 2.  | With           | a regard to any nucleotide and/or amino acid sequence disclosed in the international application and neces<br>ntion, this opinion has been established on the basis of:                                  | sary to the elamon    |
|     | a.             | type of material   |                       |
|     |                | a sequence listing   | v.*                   |
|     |                | table(s) related to the sequence listing   |                       |
|     | b.             | format of material   |                       |
|     |                | in written format  |                       |
|     |                | in computer readable form  |                       |
|     | c.             | time of filing/furnishing  |                       |
| ŀ   |                | contained in the international application as filed.   |                       |
|     |                | filed together with the international application in computer readable form.   |                       |
|     |                | furnished subsequently to this Authority for the purposes of search.   |                       |
|     | $\overline{}$  | In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating them.   | eto has been filed or |
| 3.  | Ш              | In addition, in the case that more than one version of copy of a sequent or additional copies is identical to that filed or does not go beyond the application as filed, as appropriate, were furnished. | in the application as |
|     |                | filed or does not go beyong the apprication as thed, as appropriate, were tolinated.   |                       |
| 4.  | ∧ddi           | litional comments:   |                       |
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## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/001102

| 1.  | No. V Reasoned statemer   | n under Ku   | le 43bis.1(a)(i) with regard to  | noverty, inventive step of it   | naustrial applicability;   |                      |
|-----|---|--|--|---|--|----------------------|
| ,   | citations and expla   | nations sup  | porting such statement   |   |  |                      |
| 1.  | Statement   |  |  |   |  |                      |
|     | Novelty (N)   | Clair.   | 1 – 4  |   | ,  | YES                  |
|     |   | Claims   |  |   |  | NO                   |
|     |   | Claims   |  |   | · · · · · · · · · · · · · · · · · · ·  | 110                  |
| ~   | Inventive step (IS)   | Claims   |  | •   |  | YES                  |
|     |   |  | 1-4  | ,   |  | NO                   |
|     |   | •  |  |   | ,  |                      |
|     | Industrial applicability (IA)   | Claims   | 1-4  |   |  | YES                  |
|     | •   | Claims   |  |   | <u> </u>   | NO                   |
|     | ·   |  |  |   |  |                      |
| 2.  | Citations and explanations:   |  |  |   | ,  |                      |
| , • | Claims, Industrial Field  Document 3: US, 2003/   |  |  |   |  |                      |
|     | ISR.  Document 1 or 2 sulfonic group as an age like.  Document 3 des cardiovascular diseases describe that inflammat diseases, and that vasod  The subject mat and treatments for cardi same drug may be applifasudil can be used for trused in conjunction will  | 2 describes an related to influence of decoracion according ters of decoracion according term of the prevent other dras describes ubject med in docu | a agent and composition of inflammations included in a grant and bypass opeoch as fasudil can be used in diseases. Therefore, from a grant and treatments rugs.  The disease of companying the companying of and treatments rugs.  The disease of companying of the companying of and treatments rugs. | an isoquinoline derivatments for vascular of the prevention of ing cyclooxygenase I ration is included amed in the said method common technical from the description of ing a bypass operation of the cardiovascular derson skilled in the arguing an isoquinolin | rative containing a dilation, angina and the of and treatments for Therefore, claims 1 and cong cardiovascular d. The prevention of document 3, while in, it can be seen that is eases, albeit it has to the could have easily the derivative containing and the containing and treatment and the could have easily the derivative containing and the could have easily the derivative containing and the could have easily the derivative containing and the could have easily the could have easily the containing and the could have easily the containing and the could have easily the containing and the could have easily the coul | -4 on (the           |
| -   | Claims 1-4 do n ISR.  Document 1 or sulfonic group as an age like.  Document 3 des cardiovascular diseases describe that inflammati diseases, and that vasod  The subject mat and treatments for cardi same drug may be appli fasudil can be used for t used in conjunction with  Consequently, a conceived deriving the s sulfonic group describes | 2 describes an related to influence of decoracion according ters of decoracion according term of the prevent other dras describes ubject med in docu | es the effectiveness of a prevention of and treat agent and composition inflammations including anying a bypass opeing a fasudil can be us ocuments 1-3 involve a diseases. Therefore, from a fammation accompanyintion of and treatments rugs.  | an isoquinoline derivatments for vascular of the prevention of ing cyclooxygenase I ration is included amed in the said method common technical from the description of ing a bypass operation of the cardiovascular derson skilled in the arguing an isoquinolin | rative containing a dilation, angina and the of and treatments for Therefore, claims 1 and cong cardiovascular d. The prevention of document 3, while in, it can be seen that is eases, albeit it has to the could have easily the derivative containing and the containing and treatment and the could have easily the derivative containing and the could have easily the derivative containing and the could have easily the derivative containing and the could have easily the could have easily the containing and the could have easily the containing and the could have easily the containing and the could have easily the coul | he -4 th             |
|     | Claims 1-4 do n ISR.  Document 1 or sulfonic group as an age like.  Document 3 des cardiovascular diseases describe that inflammati diseases, and that vasod  The subject mat and treatments for cardi same drug may be appli fasudil can be used for t used in conjunction with  Consequently, a conceived deriving the s sulfonic group describes | 2 describes an related to influence of decoracion according ters of decoracion according term of the prevent other dras describes ubject med in docu | es the effectiveness of a prevention of and treat agent and composition inflammations including anying a bypass opeing a fasudil can be us ocuments 1-3 involve a diseases. Therefore, from a fammation accompanyintion of and treatments rugs.  | an isoquinoline derivatments for vascular of the prevention of ing cyclooxygenase I ration is included amed in the said method common technical from the description of ing a bypass operation of the cardiovascular derson skilled in the arguing an isoquinolin | rative containing a dilation, angina and the of and treatments for Therefore, claims 1 and cong cardiovascular d. The prevention of document 3, while in, it can be seen that is eases, albeit it has to the could have easily the derivative containing and the containing and treatment and the could have easily the derivative containing and the could have easily the derivative containing and the could have easily the derivative containing and the could have easily the could have easily the containing and the could have easily the containing and the could have easily the containing and the could have easily the coul | he<br>-4<br>on<br>th |
|     | Claims 1-4 do n ISR.  Document 1 or sulfonic group as an age like.  Document 3 des cardiovascular diseases describe that inflammati diseases, and that vasod  The subject mat and treatments for cardi same drug may be appli fasudil can be used for t used in conjunction with  Consequently, a conceived deriving the s sulfonic group describes | 2 describes an related to influence of decoracion according ters of decoracion according term of the prevent other dras describes ubject med in docu | es the effectiveness of a prevention of and treat agent and composition inflammations including anying a bypass opeing a fasudil can be us ocuments 1-3 involve a diseases. Therefore, from a fammation accompanyintion of and treatments rugs.  | an isoquinoline derivatments for vascular of the prevention of ing cyclooxygenase I ration is included amed in the said method common technical from the description of ing a bypass operation of the cardiovascular derson skilled in the arguing an isoquinolin | rative containing a dilation, angina and the of and treatments for Therefore, claims 1 and cong cardiovascular d. The prevention of document 3, while in, it can be seen that is eases, albeit it has to the could have easily the derivative containing and the containing and treatment and the could have easily the derivative containing and the could have easily the derivative containing and the could have easily the derivative containing and the could have easily the could have easily the containing and the could have easily the containing and the could have easily the containing and the could have easily the coul | he<br>-4<br>th       |
|     | Claims 1-4 do n ISR.  Document 1 or sulfonic group as an age like.  Document 3 des cardiovascular diseases describe that inflammati diseases, and that vasod  The subject mat and treatments for cardi same drug may be appli fasudil can be used for t used in conjunction with  Consequently, a conceived deriving the s sulfonic group describes | 2 describes an related to influence of decoracion according ters of decoracion according term of the prevent other dras describes ubject med in docu | es the effectiveness of a prevention of and treat agent and composition inflammations including anying a bypass opeing a fasudil can be us ocuments 1-3 involve a diseases. Therefore, from a fammation accompanyintion of and treatments rugs.  | an isoquinoline derivatments for vascular of the prevention of ing cyclooxygenase I ration is included amed in the said method common technical from the description of ing a bypass operation of the cardiovascular derson skilled in the arguing an isoquinolin | rative containing a dilation, angina and the of and treatments for Therefore, claims 1 and cong cardiovascular d. The prevention of document 3, while in, it can be seen that is eases, albeit it has to the could have easily the derivative containing and the containing and treatment and the could have easily the derivative containing and the could have easily the derivative containing and the could have easily the derivative containing and the could have easily the could have easily the containing and the could have easily the containing and the could have easily the containing and the could have easily the coul | he -4 th             |